Evaluating Men With Benign Prostatic Hyperplasia

Herbert Lepor, MD

Department of Urology, New York University School of Medicine, New York, NY

The clinical manifestations of benign prostatic hyperplasia (BPH) include lower urinary tract symptoms (LUTS), poor bladder emptying, urinary retention, detrusor instability, urinary tract infection, hematuria, and renal insufficiency. However, the majority of men with BPH present with LUTS only. Because LUTS can indicate a variety of conditions, evaluation of symptomatic men must first aim to identify or exclude BPH and, if present, assess its severity. It is important to assess symptom severity at baseline and during follow-up, using the American Urological Association Symptom Index or the International Prostate Symptom Score. Further testing can then be tailored to narrow the diagnosis and guide treatment decisions. Factors such as patient age and concomitant malignancy will also affect management, but the main goal of treatment remains the improvement of quality of life for the patient.
[Rev Urol. *2004;6(suppl 1):S8-S15*]

Key words: Benign prostatic hyperplasia • Prostate-specific antigen • American Urological Association Symptom Index • International Prostate Symptom Score

The term benign prostatic hyperplasia (BPH) has different connotations to the pathologist, urodynamicist, practicing urologist, and patient. To the pathologist, BPH is a microscopic diagnosis characterized by cellular proliferation of the stromal and epithelial elements of the prostate.[1] To the practicing urologist, it represents a constellation of lower urinary tract symptoms (LUTS) that develop in the male population in association with aging and prostatic enlargement, presumably

caused by bladder outlet obstruction (BOO).[2] To the urodynamicist, the hallmark of BPH is the observation of synchronous elevated voiding pressure and a low urinary flow rate in the absence of other disease processes that cause BOO.[3] The patient is typically concerned about the impact of BPH on quality of life rather than the presence of cellular proliferation, prostatic enlargement, or elevated voiding pressures.

Because of the diverse connotations associated with the term, it is necessary to define BPH as microscopic BPH, macroscopic BPH, or clinical BPH. Microscopic BPH represents histologic evidence of cellular proliferation of the prostate. Macroscopic BPH refers to enlargement of the prostate resulting from microscopic BPH. Clinical BPH represents the LUTS, bladder dysfunction, hematuria, and urinary tract infection (UTI) resulting from macroscopic BPH. Abrams[4] has suggested using the more clinically descriptive terms benign prostatic enlargement (BPE), BOO, and LUTS to replace BPH.

Microscopic BPH describes a proliferative process of the stromal and epithelial elements of the prostate.[5] The proliferative process originates in the transition zone and the periurethral glands.[6] It is rarely identified in men younger than 40 years.[7] The autopsy incidence of BPH is age-dependent, with the proliferative process being present in approximately 70% and 90% of men in their seventh and ninth decades of life, respectively. The development of microscopic BPH requires aging and the testes as the source of androgens.[8] Androgens play a passive role in the proliferative process. The specific biochemical event that initiates and promotes microscopic BPH has yet to be identified and characterized. Growth factors presumably are involved through autocrine and paracrine stromal epithelial interactions.[9]

Macroscopic BPH denotes an "enlarged" prostate. Digital rectal examination (DRE) provides a relatively crude estimate of prostate size compared with measurements obtained using transrectal ultrasonography (TRUS).[10] Although knowledge of prostate size may be clinically relevant in some cases, justifying the cost of obtaining a precise measurement of gland volume in all cases is questionable. A strong correlation exists between serum prostate-specific antigen (PSA) levels and prostate volume.[11] There is no consensus regarding the extent of enlargement required to establish the diagnosis of macroscopic BPH. There is evidence that men with prostate volumes exceeding 40 cm^3 have a greater response to 5-α-reductase inhibitors.[12] Therefore, some experts limit the diagnosis of BPH to men with prostate volumes exceeding 40 cm^3.

The specific biochemical event that initiates and promotes microscopic BPH has yet to be identified and characterized.

The clinical manifestations of BPH include LUTS, poor bladder emptying, urinary retention, detrusor instability, UTI, hematuria, and renal insufficiency.[13] The overwhelming majority of men present with LUTS only. Historically, the pathophysiology of clinical BPH was attributed to BOO secondary to macroscopic enlargement of the prostate gland.[14] This hypothesis was supported by epidemiologic data suggesting that the prevalence of microscopic BPH, macroscopic BPH, and clinical BPH is age-dependent and, therefore, causally related.[15] This simplistic concept of the pathophysiology of BPH has been challenged by more recent reports demonstrating weak relationships among prostate size, severity of BOO, and severity of symptoms.[16-19]

BPH: Differential Diagnosis

The complex of symptoms now commonly referred to as LUTS and previously termed "prostatism" is not specific for BPH. Aging men with a variety of lower urinary tract pathologies may exhibit similar, if not identical, symptoms (Table 1).

The initial diagnostic challenge in patients presenting with LUTS is to establish that the symptoms are due to BPH. This is the primary focus of the initial evaluation and diagnostic testing. Fortunately, nonprostatic causes of symptoms can be excluded for the majority of patients on the basis of history, physical examination, and urinalysis results. Additional diagnostic testing is necessary in patients for whom the diagnosis is still unclear after the initial evaluation.

Objectives of Diagnostic Evaluation

The primary objective of the diagnostic evaluation of men with LUTS is to exclude other urologic and non-urologic conditions that may masquerade as BPH. A secondary objective is to determine the severity of BPH. How severe and bothersome are the symptoms? How large is the prostate? Is there associated hematuria and UTI? Is there evidence of bladder dysfunction manifested by incomplete bladder emptying and detrusor instability? Is the prostatic enlargement causing significant BOO?

Men older than 50 years are at risk for clinical BPH and may have coexisting conditions mimicking BPH. Therefore, all men older than 50 years should undergo an evalua-

Table 1
Differential Diagnosis of Lower Urinary Tract Symptoms

Prostate
• Benign prostatic hyperplasia
• Prostatitis
• Prostate cancer
Bladder
• Bladder cancer
• Bladder stones
• Overactive bladder
• Interstitial cystitis
• Primary bladder neck hypertrophy
• Radiation cystitis
Urethral
• Urethritis
– Gonococcal
– Non-gonococcal
• Urethral stricture
Neurologic and spinal cord
• Parkinson disease
• Multiple sclerosis
• Cerebrovascular accident
• Spinal cord trauma
• Lumbosacral disc disease
Urinary tract infection
• Bacterial
• Tuberculosis
• Viral
• Fungal
Metabolic
• Adult-onset diabetes mellitus
• Nephrogenic diabetes insipidus
Pharmacologic agents
• Diuretics
• α-Agonists
• Anticholinergics
Pelvic surgery

tion that includes determination of the American Urological Association (AUA) symptom score and a detailed medical history, a DRE, a urinalysis, and a serum PSA measurement. Urinary cytologies, TRUS of the prostate, uroflowmetry, postvoid residual urine volume (PVR) measurement, pressure-flow urodynamics, and filling cystometry are optional studies that should be performed with a specific purpose as related to confirming the diagnosis, evaluating the severity of BPH, or selecting treatment.

Initial Evaluation

The Agency for Health Care Policy and Research[20] and the International Consultation on BPH[21] have published recommendations for the initial evaluation of BPH using an evidence-based approach.

Medical History

A detailed medical history focusing on the urinary tract, previous surgical procedures, general health issues, and fitness for possible surgical procedures must be obtained. Specific things to discuss when taking the history of a man with BPH symptoms include a history of hematuria, UTI, tuberculosis, diabetes, nervous system and spinal disease (eg, Parkinson disease or stroke), prior radiation or pelvic surgery, urethral stricture disease, urinary retention, and aggravation of symptoms by cold or sinus medications. Prescription and over-the-counter medications being taken by the patient should be examined to determine whether they can impair bladder contractility (anticholinergics), increase bladder outflow resistance (α-agonists), or alter urine production (diuretics). A history of prior lower urinary tract surgery raises the possibility of urethral stricture or bladder neck contracture. Use of a voiding diary (recording times and volumes) may help identify patients with polyuria or other nonprostatic disorders.

Physical Examination

A DRE and a focused neurologic examination must be performed. In addition, the external genitalia should be examined to exclude meatal stenosis or a palpable urethral mass. Abdominal examination is necessary to exclude a distended, palpable bladder. The DRE and neurologic examination are performed to detect prostate or rectal malignancy, evaluate anal sphincter tone, and rule out any neurologic problems that may cause the presenting symptoms. The presence of prostatic induration is as important a finding as the presence of a nodule.

DRE establishes the approximate size of the prostate gland.[10] In patients who choose or require invasive therapy, estimation of prostate size is an important factor in determining the most appropriate technical approach. DRE provides a sufficiently accurate measurement in most cases. The size of the prostate should not be considered when deciding whether active treatment is required; rather, the size of the prostate should influence decisions regarding whether to consider prescribing a 5-α-reductase inhibitor to relieve LUTS and prevent progression to acute urinary retention or whether to perform a transurethral versus an open prostatectomy.

Urinalysis

A urinalysis must be done either by using a dipstick test or by examining the spun sediment to evaluate glucosuria and to rule out UTI and hematuria. The presence of UTI or hematuria requires additional testing to exclude genitourinary malignancies and other conditions unrelated to BPH. Urine cytology should be considered in men with severe irritable symptoms, especially if they have a history of smoking. If a dipstick approach is used, the test should include leukocyte esterase and nitrite tests for the detection of pyuria and bacteriuria.

There is insufficient evidence to support urinalysis as an effective screening procedure in asympto-

matic men.[22] Because serious urinary tract disorders are relatively uncommon, the positive predictive value of screening for them is low, and the effectiveness of early detection and intervention is unproven. However, in older men with BPH, who have a higher prevalence of these disorders, the benefits of an innocuous test such as urinalysis clearly outweigh the harm involved. The test permits the selective use of renal imaging and endoscopy for patients with the greatest chance of benefiting from these procedures. More important, urinalysis assists in distinguishing diabetes, UTIs, and bladder cancer from BPH. These conditions may produce urinary tract symptoms (such as frequency and urgency) that mimic BPH.

Serum Creatinine Measurement

The measurement of serum creatinine has been recommended in the initial evaluation of all patients with LUTS to exclude renal insufficiency caused by the presence of obstructive uropathy. However, in men with an elevated serum creatinine level, the etiology is rarely associated with acute or chronic urinary retention secondary to BPH. Obtaining a serum creatinine measurement may be an appropriate screen for renal disease unrelated to BPH.

Serum PSA Measurement

Advanced prostate cancer can lead to LUTS by producing urethral obstruction similar to that in men with BPH. In men with clinically localized cancer, the distribution of AUA symptom scores is similar to that in age-matched men in the general population, suggesting that it is the BPH that causes the symptoms.[23] Prostate cancer commonly coexists with BPH and, in most men with a 10-year or longer life expectancy, a finding of concomitant prostate cancer may well alter management of the BPH component. The detection of a large nodular prostate cancer on DRE would no doubt alter therapy; however, the "early detection" of small-volume prostate cancer in an 80-year-old man is unlikely to be beneficial. A PSA test and DRE increase the detection rate of prostate cancer over DRE alone. Therefore, measurement of the serum PSA value should be performed in patients for whom the identification of cancer would clearly alter BPH management.

There is significant overlap between the serum PSA values of men with BPH and those of men with clinically localized prostate cancer. Twenty-eight percent of men with histologically proven BPH have a serum PSA level greater than 4.0 ng/mL.[20] Serum PSA trends over time (PSA velocity), measurement of free versus complexed PSA, and PSA density may help to improve the specificity of PSA testing in men with BPH. McConnell and colleagues[24] have demonstrated a strong correlation between prostate volume and serum PSA levels. Therefore, PSA level may represent an acceptable proxy for prostate volume measurement when selecting candidates for 5-α-reductase inhibitor therapy.

There is a special concern relating to men with BPH treated with 5-α-reductase inhibitors: Because these agents reduce serum PSA levels an average of 50% after 3 to 6 months of therapy, failure to establish a baseline (pretreatment) PSA level complicates the interpretation of future PSA values.

Symptom Assessment

The International Prostate Symptom Score (IPSS), which is similar to the AUA Symptom Index,[25] is recommended as the symptom scoring instrument to be used for the baseline assessment of symptom severity in men presenting with LUTS. The difference between the AUA symptom score and the IPSS is that the latter incorporates a question capturing the global impact of LUTS on quality of life. When the IPSS is used, symptoms can be classified as mild (score, 0-7), moderate (score, 8-19), or severe (score, 20-35). The symptom score should also be the primary determinant of treatment response or disease progression in the follow-up period.

The IPSS cannot be used to establish the diagnosis of BPH. Men (and women) with a variety of lower urinary tract disorders (eg, infection, tumor, neurogenic bladder disease) will also have high IPSSs. However, the IPSS is the ideal instrument to grade baseline symptom severity, assess response to therapy, and detect symptom progression in men managed with watchful waiting. Optimal treatment decisions for individual patients also need to take into account how a given level of symptoms affects each patient's quality of life (bothersomeness).

Measurement of the serum PSA value should be performed in patients for whom the identification of cancer would clearly alter BPH management.

Clearly, symptom scores alone do not capture the morbidity of a prostate problem as perceived by the individual patient. The impact of symptoms on a patient's lifestyle must also be considered. An intervention may make more sense for a moderately symptomatic patient who finds his symptoms highly bothersome than for a severely symptomatic patient who finds his symptoms tolerable.

Transrectal Ultrasonography

TRUS provides a more accurate

assessment of prostate volume than does DRE. In most cases, a precise prostate volume measurement is not necessary for the evaluation of LUTS or selection of therapy.

Prostate volume is an important consideration when determining if a transurethral prostatectomy is technically feasible. Most surgeons are comfortable resecting upwards of 50 g of prostatic tissue with this method. More than 90% of prostatectomies can be performed via the transurethral route. Very large prostates are more safely approached using an open surgical technique. In selected cases in which the prostate is very large on DRE, a TRUS should be performed in order to determine the optimal approach to prostatectomy.

5-α-Reductase inhibitors relieve LUTS presumably by reducing prostate volume. It is therefore intuitive that men with LUTS and small prostates are not likely to respond to 5-α-reductase inhibitor therapy. In general, 5-α-reductase inhibitors should be offered to men with moderate-size or large prostates (>40 cm^3). However, because 40 cm^3 is an arbitrary cutoff point, precise knowledge of prostate volume is not necessary before prescribing a 5-α-reductase inhibitor.

Uroflowmetry

Uroflowmetry is the electronic recording of the urinary flow rate throughout the course of micturition. The results of uroflowmetry are nonspecific for causes of the symptoms. For example, an abnormally low flow rate may be caused by BOO (eg, hyperplastic prostate, urethral stricture, meatal stenosis) or by detrusor hypocontractility. Flow rate measurements are inaccurate if the voided volume is less than 150 mL. There is no consensus as to the maximum flow rate (Q_{max}) "cut point" discriminating obstruction from non-obstruction. Q_{max} values suggestive of BOO range from 12 mL/s to 15 mL/s.

Q_{max} appears to have limited ability in predicting surgical outcomes or response to medical therapy. In a study by Jensen and colleagues,[26] 53 patients underwent prostatectomy based on clinical indication alone. All 3 groups of subjects stratified according to level of Q_{max} experienced improvements in their symptom score after surgery. The patients who had a Q_{max} of less than 10 mL/s before treatment had a better overall subjective outcome as assessed by global subjective judgment. Lepor and colleagues[27] reported that response to an α_1-blocker was independent of baseline Q_{max}.

Small, portable, 3-dimensional ultrasound devices are widely used to measure PVR in the office setting.

Postvoid Residual Urine Volume

PVR is the volume of fluid remaining in the bladder immediately after the completion of micturition. Studies indicate that residual urine volume normally ranges from 0.09 mL to 2.24 mL, with the mean being approximately 0.53 mL.[28] Seventy-eight percent of healthy men have PVRs of less than 5 mL, and 100% have volumes of less than 12 mL.[29]

PVR measurement can be performed by noninvasive (ultrasonography) or invasive (catheterization) methods. The most common method is ultrasonography. Small, portable, 3-dimensional ultrasound devices (BladderScan™, Diagnostic Ultrasound, Bothell, Wash) are widely used to measure PVR in the office setting. The reported accuracy of these devices is comparable to that of more expensive ultrasound units and catheterization. In one study, the correlation coefficient between PVR as determined by catheterization versus ultrasonography with a portable device was 0.79.[30] Over the years, the clinical performance of this 3-dimensional technology has evolved to outperform large, stationary ultrasound.[31]

Birch and colleagues[32] reported that, of 30 men with BPH, 66% had wide variations in PVR when 3 measurements were taken on the same day. In 34% of subjects, there was no difference among the 3 measurements. In 58% of subjects, at least 2 volumes were significantly different. In 8% of patients, all 3 volumes were different. In most patients, 2 measurements were statistically similar, whereas the third yielded quite different results.

Bruskewitz and colleagues[33] found similarly wide variations of measured volumes when repeated measurements of PVR (repeated 2 to 5 times) were performed by in-and-out catheterization in 47 men before prostatectomy. They also found no correlation between the amount of residual urine and any cystoscopic or urodynamic findings, symptoms, or the presence or absence of a history of UTIs. In the AUA Outcome Study, Barry and colleagues[16] found a significant correlation between high PVR and low flow rates but no correlation with IPSS. Therefore, large PVRs may exist in men who have minimal symptoms.

Large PVRs may exist in men who have minimal symptoms.

Traditionally, urologists have assumed that increasing PVRs denote

significant bladder dysfunction and risk of developing UTI. This concept underlies the common inclusion of PVR measurement in the evaluation of men with BPH. The precise consequences of PVR have not been critically examined longitudinally. Therefore, the threshold PVR that warrants clinical concern is unknown.

Pressure-Flow Studies

Pressure-flow studies differentiate between patients with a low Q_{max} secondary to obstruction and those in whom a low Q_{max} is caused by a decompensated or neurogenic bladder. Pressure-flow studies correlate poorly with severity of LUTS,[3] implying that some men with high levels of BOO are symptomatic and that men with no BOO may have severe LUTS. Therefore, pressure-flow studies are limited in determining the cause of LUTS. Pressure-flow studies may identify high-pressure obstruction in symptomatic men with normal flow rates.

Evidence for the usefulness of pressure-flow studies to predict surgical failure is equivocal. Some investigations have reported reduced failure rates, whereas others have reported that pressure-flow studies performed no better than Q_{max} measurements in this regard. Some patients who are excluded from surgery based on the pressure-flow test may benefit from symptom relief following surgery.

Pressure-flow studies should be performed when the distinction between urethral obstruction and impaired contractility will affect therapeutic decision making. Patients with a history of neurologic diseases known to affect bladder or sphincteric functions, as well as patients with normal flow rates (Q_{max} >15 mL/s) but bothersome symptoms, may also benefit from urodynamic evaluation, especially if surgical therapy is contemplated.

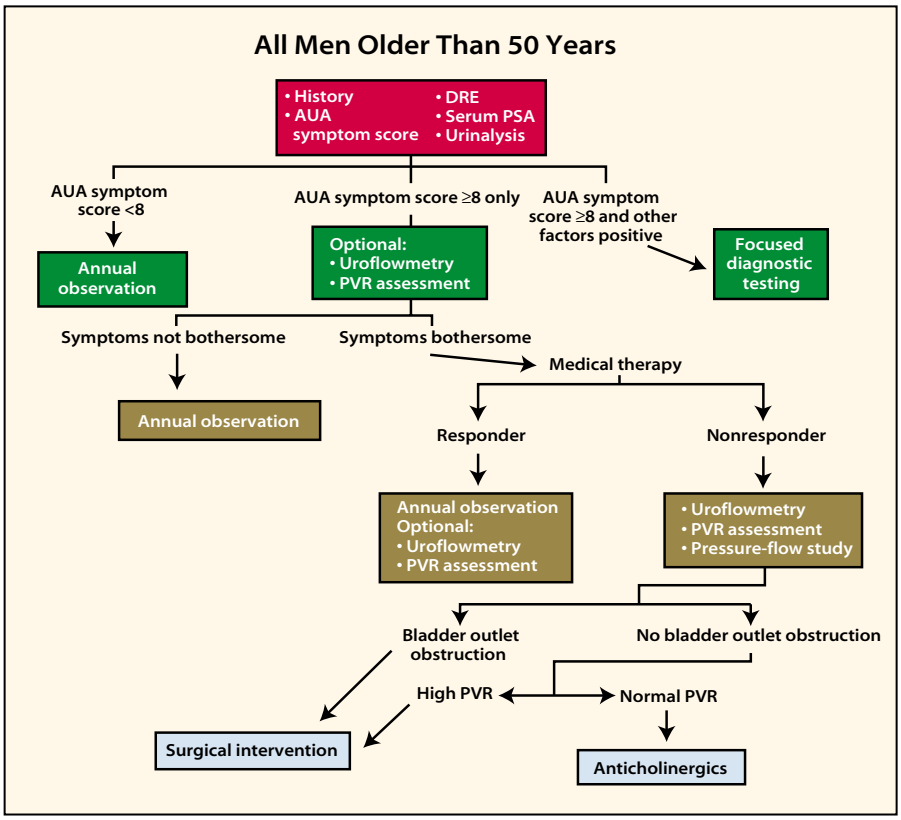

Figure 1. *An algorithm for the evaluation of men with benign prostatic hyperplasia. AUA, American Urological Association; DRE, digital rectal examination; PSA, prostate-specific antigen; PVR, postvoid residual urine volume.*

The value of pressure-flow plots is acknowledged by many urodynamic experts. The test/retest reliability of pressure-flow studies appears to be reasonable.[34] However, there is little standardization in interpretation of these plots and somewhat arbitrary cutoff values for defining obstruction as opposed to non-obstruction. Investigators have proposed various ways to present the same sets of data and claim superior differentiation between patient groups.[35-38] This variability in data presentation and definition has made it difficult to analyze the evidence that supports the use of pressure-flow studies.

The natural history of significant BOO is also poorly defined. Although one assumes that BOO must ultimately cause irreparable detrusor damage, this has yet to be proved. Therefore, an isolated finding of BOO is not sufficient cause to pursue intervention. Because a diagnosis of BOO is relevant only in the presence of symptoms, pressure-flow studies have limited clinical utility.

Pressure-flow studies provide much more specific insight into detrusor function and the etiology of voiding dysfunction than do flow rate measurements. However, a number of outcome-based investigations demonstrate only a modest additional value of pressure-flow studies over symptom and flow rate evaluation.

Filling Cystometry (Cystometrography)

Filling cystometry adds limited information to the evaluation of most men with LUTS and is not recommended in routine cases. The test may have value in the evaluation of

patients with known or suspected neurologic lesions and LUTS, but pressure-flow studies provide more specific information.

Filling cystometry, an invasive urodynamic study, provides information on bladder capacity, the presence and threshold of uninhibited detrusor contractions (UDCs), and bladder compliance. UDCs are present in approximately 60% of men with LUTS and correlate strongly with irritative voiding symptoms. However, UDCs resolve in most patients after prostatectomy. Only about one fourth of patients who have UDCs before treatment continue to have them afterward. Patients whose symptoms do not improve after surgery are more likely to have persistent UDCs; however, preoperative cystometrography does not help identify these patients.

Urethroscopy/Imaging of the Upper Urinary Tract

Urethroscopy and imaging of the upper urinary tract should be performed only if the LUTS are accompanied by a UTI, hematuria, or a positive urinary cytologic finding. Men with LUTS and no evidence of hematuria are at no greater risk for renal tumors or other upper tract abnormalities. There are no endoscopic findings that link LUTS to a prostatic origin.

An Algorithm for the Evaluation of Men With BPH

Figure 1 presents an algorithm for the evaluation of men with BPH. All men older than 50 years should undergo an annual examination by a primary care physician that includes a comprehensive review of LUTS (using the AUA Symptom Index), DRE, urinalysis, and serum PSA measurement. If the AUA symptom score is less than 8 (mild symptoms), annual observation is recommended. If the AUA symptom score is 8 or greater (moderate/severe symptoms) and the serum PSA measurement, DRE, and urinalysis results are normal, uroflowmetry and PVR measurement may be performed in the office setting to determine if there is evidence of significant BOO and bladder dysfunction. These tests are optional, as their benefits are unproven. If the urinalysis, DRE, or PSA measurement is abnormal, additional testing is warranted.

If the patient's symptoms are not bothersome, annual observation is recommended. If the symptoms are bothersome, medical therapy typically represents first-line intervention. If medical therapy is effective, annual observation is recommended, which may include uroflowmetry and PVR measurement. If medical therapy is ineffective, uroflowmetry, PVR measurement, and a urodynamic pressure-flow study should be performed. If there is no BOO and PVR is normal, one may consider anticholinergic therapy, especially if there is evidence of an overactive bladder. If PVR is high, surgical intervention should be considered, even in the absence of BOO. ■

References

1. Strandberg JD. Comparative pathology of benign prostatic hyperplasia. In: Lepor H, ed. *Prostatic Diseases*. Philadelphia: WB Saunders; 2000:329-343.
2. Shapiro E, Lepor H. Pathophysiology of clinical

Main Points

- The primary objective of the diagnostic evaluation of men with lower urinary tract symptoms (LUTS) is to exclude other urologic and non-urologic conditions that may masquerade as benign prostatic hyperplasia (BPH). A secondary objective is to determine the severity of BPH.
- Men older than 50 years are at risk for clinical BPH and may have coexisting conditions that mimic BPH. Therefore, all men older than 50 years should undergo an evaluation that includes determination of the American Urological Association (AUA) symptom score, a detailed medical history taking, digital rectal examination, urinalysis, and serum prostate-specific antigen (PSA) measurement.
- Prostate cancer commonly coexists with BPH and, in most men with a 10-year or longer life expectancy, a finding of concomitant prostate cancer may well alter the management of the BPH component. Therefore, measurement of the serum PSA value should be performed in patients for whom the identification of cancer would clearly alter BPH management.
- Baseline symptom severity should be determined in men presenting with LUTS using the AUA symptom score or the International Prostate Symptom Score (IPSS). The difference between the AUA symptom score and the IPSS is that the latter incorporates a question capturing the global impact of LUTS on quality of life.
- Postvoid residual urine volume (PVR) measurement can be performed by noninvasive (ultrasonography) or invasive (catheterization) methods. The availability of small, portable ultrasonography devices has facilitated PVR measurement in the office setting. The threshold PVR that warrants clinical concern is not yet known.
- Pressure-flow studies should be performed when the distinction between urethral obstruction and impaired contractility will affect therapeutic decision making. Filling cystometry adds limited information to the evaluation of most men with LUTS and is not recommended in routine cases.

benign prostatic hyperplasia. *Urol Clin North Am*. 1995;22:285-290.
3. Nitti VW. Diagnosis of obstructive uropathy. In: Lepor H, ed. *Prostatic Diseases*. Philadelphia: WB Saunders; 2000:197-209.
4. Abrams P. In support of pressure-flow studies for evaluating men with lower urinary symptoms. *Urology*. 1994;44:153-155.
5. Bartsch G, Muller HR, Oberholzer M, et al. Light microscopic stereological analysis of the normal human prostate and of benign prostatic hyperplasia. *J Urol*. 1979;122:487-491.
6. McNeal JG. The prostate gland: morphology and pathobiology. *Monogr Urol*. 1983;4:3-33.
7. Berry SJ, Coffey DS, Walsh PC, Ewing LL. The development of human prostatic hyperplasia with age. *J Urol*. 1984;132:474-479.
8. Walsh PC. Benign prostatic hyperplasia. In: Walsh PC, Gittes RF, Perlmutter AD, Stamey TA, eds. *Campbell's Urology*. 5th ed. Philadelphia: WB Saunders; 1986:1248-1265.
9. Steiner MS. Molecular biology of prostate growth regulation. In Lepor H, ed. *Prostatic Diseases*. Philadelphia: WB Saunders; 2000:41-57.
10. Roehrborn CG, Girman CJ, Rhodes T, et al. Correlation between prostate size estimated by digital rectal examination and measured by transrectal ultrasound. *Urology*. 1997;49:548-557.
11. Roehrborn CG, Boyle P, Gould AL, et al. Serum prostate-specific antigen as a predictor of prostate volume in men with benign prostatic hyperplasia. *Urology*. 1999;53:581-589.
12. Boyle P, Gould AL, Roehrborn CG. Prostate volume predicts outcome of treatment of benign prostatic hyperplasia with finasteride: meta-analysis of randomized clinical trials. *Urology*. 1996;48:398-405.
13. Jepsen JV, Bruskewitz RC. Clinical manifestations and indications for treatment. In: Lepor H, ed. *Prostatic Diseases*. Philadelphia: WB Saunders; 2000:127-142.
14. Lepor H. α-Adrenergic blockers for the treatment of benign prostatic hyperplasia. In: Lepor H, ed. *Prostatic Diseases*. Philadelphia: WB Saunders; 2000:297-307.
15. Isaacs JT, Coffey DS. Etiology and disease process of benign prostatic hyperplasia. *Prostate Suppl*. 1989;2:33-50.
16. Barry MJ, Cockett AT, Holtgrewe HL, et al. Relationship of symptoms of prostatism to commonly used physiological and anatomical measures of the severity of benign prostatic hyperplasia. *J Urol*. 1993;150:351-358.
17. Bosch J, Kranse R, Van Mastrigt R, et al. Reasons for the weak correlation between prostate volume and urethral resistance parameters in patients with prostatism. *J Urol*. 1995;153:689-693.
18. Girman CJ, Jacobsen SJ, Guess HA, et al. Natural history of prostatism: relationship among symptoms, prostate volume and peak urinary flow rate. *J Urol*. 1995;153:1510-1515.
19. Yalla SV, Sullivan MP, Lecamwasam HS, et al. Correlation of American Urological Association Symptom Index with obstructive and nonobstructive prostatism. *J Urol*. 1995;153:674-680.
20. McConnell JD, Barry MJ, Bruskewitz RC, et al. Benign prostatic hyperplasia: diagnosis and treatment. *Clinical Practice Guideline No 8*. Rockville, Md: Agency for Health Care Policy and Research, US Dept of Health and Human Services; 1994. AHCPR publication 94-0582.
21. Denis L, Griffiths K, Khoury S, et al, eds. *Proceedings of the 4th International Consultation on BPH*. Plymouth, UK: Health Publication Ltd; 1998.
22. Preventive Services Task Force (US). *Guide to Clinical Preventive Services: An Assessment of the Effectiveness of 169 Interventions*. Baltimore, Md: Williams & Wilkins; 1989:419.
23. Schwartz EJ, Lepor H. Radical retropubic prostatectomy reduces symptom scores and improves quality of life in men with moderate and severe lower urinary tract symptoms. *J Urol*. 1999;161:1185-1188.
24. McConnell JD, Bruskewitz R, Walsh P, et al. The effect of finasteride on the risk of acute urinary retention and the need for surgical treatment among men with benign prostatic hyperplasia. *N Engl J Med*. 1998;338:557-563.
25. Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association Symptom Index for benign prostatic hyperplasia. *J Urol*. 1992;148:1549-1557.
26. Jensen KM, Bruskewitz RC, Iversen P, Madsen PO. Spontaneous uroflowmetry in prostatism. *Urology*. 1984;24:403-409.
27. Lepor H, Williford WO, Barry MJ, et al. The impact of medical therapy on bother due to symptoms, quality of life and global outcome, and factors predicting response. *J Urol*. 1998; 160:1358-1367.
28. Hinman F Jr, Cox CE. Residual urine volume in normal male subjects. *J Urol*. 1967;97:641-645.
29. Di Mare Jr, Fish SR, Harper JM, Politano VA. Residual urine in normal male subjects. *J Urol*. 1963;96:180-181.
30. Ireton RC, Krieger JN, Cardenas DD, et al. Bladder volume determination using a dedicated, portable ultrasound scanner. *J Urol*. 1990;143:909-911.
31. Byun SS, Kim HH, Lee E, et al. Accuracy of bladder volume determinations by ultrasonography: are they accurate over entire bladder volume range? *Urology*. 2003;62:656-660.
32. Birch NC, Hurst G, Doyle PT. Serial residual volumes in men with prostatic hypertrophy. *Br J Urol*. 1988;62:571-575.
33. Bruskewitz RC, Iversen P, Madsen PO. Value of postvoid residual urine determination in evaluation of prostatism. *Urology*. 1982;20:602-604.
34. Rosier PF, de la Rosette JJ, Koldewijn EL, et al. Variability of pressure-flow analysis parameters in repeated cystometry in patients with benign prostatic hyperplasia. *J Urol*. 1995;153:1520-1525.
35. Abrams PH, Griffiths DJ. The assessment of prostatic obstruction from urodynamic measurements and from residual urine. *Br J Urol*. 1979;51:129-134.
36. Jensen KM, Jorgensen JB, Mogensen P. Urodynamics in prostatism. II. Prognostic value of pressure-flow study combined with stop-flow test. *Scand J Urol Nephrol Suppl*. 1988; 114:72-77.
37. Schafer W, Noppeney R, Rubben H, et al. The value of free flow rate and pressure/flow studies in the routine investigation of BPH patients. *Neurourol Urodyn*. 1988;7:219-221.
38. Schafer W, Rubben H, Noppeney R, et al. Obstructed and unobstructed prostatic obstruction: a plea for urodynamic objectivation of bladder outflow obstruction in benign prostatic hyperplasia. *World J Urol*. 1989;6:198-203.